

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

114 AAA

DATE: August 2, 1978

SUBJECT: 10182-EUP-10. TALON RODENTICIDE. Brodifacoum. Original New Anticoagulant Rodenticide. Vitamin K₁ Antagonist. ICI Americas, Inc., Wilmington, Delaware.

FROM: Roland A. Gessert, D.V.M.; Toxicology Branch

TO: Mr. Donald Stubbs, Special Registrations Section

Applicant seeks an EUP for this rodenticide, an anticoagulant vitamin K₁ antagonist. Toxicities of the technical chemical are:

Acute Oral Toxicity, male rat: LD₅₀ = 0.27 mg/kg
(For comparison purposes, LD₅₀ of Warfarin = 3 mg/kg in the rat)

Acute Oral Toxicity, female rat: LD₅₀ = 0.5 mg/kg

Oral LD ₅₀ , mouse = 0.4 mg/kg	Oral LD ₅₀ guinea pig = 2.78 mg/kg
Oral LD ₅₀ , rabbit = 0.29 mg/kg	Oral LD ₅₀ dog = 0.25 to 1 mg/kg
Oral LD ₅₀ , cat = 25 mg/kg	Oral LD ₅₀ sheep = 25 mg/kg

Toxic signs are those typical of an indirect anticoagulant. Death is due to massive internal hemorrhages, and peritoneal cavity is filled with blood.

Acute Dermal Toxicity, male rat:

LD ₅₀ in PEG 300 Carrier, 6 hours exposure	50 mg/kg
LD ₅₀ in Corn Starch Carrier, 6 hours exposure	200 mg/kg
LD ₅₀ in PEG 300 Carrier, 24 hours exposure	10 mg/kg
LD ₅₀ in Corn Starch Carrier, 24 hour exposure	50 mg/kg

Primary Skin Irritation, PEG 300 Carrier on rabbit - not a primary skin irritant

Skin Sensitization, Guinea Pig: Not a strong skin sensitizer

Acute Eye Irritation, Rabbit: Non-irritating as a 1% w/v solution in the rabbit eye

Isomer Toxicity in Male Rats & Mice: No significant difference in rate of kill or prothrombin times at acute or subacute levels between the cis and trans isomers.

Antidote Studies: Vitamin K₁ is antidotal. The minimum dose of Vitamin K₁ required to antidote a massive acute dose of the rodenticide lies between 10 and 20 mg/kg.

** Brodifacoum is: 3-[3-(4'-bromo[1,1'-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2H-1-benzopyran-2-one.

TOXICITY STUDIES WITH THE LIQUID CONCENTRATE FORMULATION (0.25% active ingredient)
USED IN MANUFACTURING THE DOSAGE FORM:

Acute Oral LD₅₀: Male Rats - 0.14 ml/kg (equiv. to 0.34 mg a.i./kg)
Female Rats - 0.13 to 0.16 ml/kg (0.32 - 0.4 mg a.i./kg)

Acute Dermal LD₅₀ in rabbits = 1 ml/kg (equiv. to 2.5 mg a.i./kg)

Acute Skin Irritation in rabbits: Slightly irritating (some erythema in
2 of 6 rabbits after 24 hours)

Skin Sensitization, guinea pig: Not a sensitizer

Acute Eye Irritation, rabbit: A mild eye irritant in unwashed eyes.

PELLET DOSAGE FORMULATION (0.005% w/w active ingredient)

Acute Oral Toxicity, rat: Calculated LD₅₀ equivalent to 7500 mg bait/kg.
(Wasn't possible to dose with pellet suspension through catheter, so
dose was calculated from the concentrate. LD₅₀ for 60 kg person is
approximately 450 grams or 1 pound of bait)

Acute Dermal Toxicity, rabbit: LD₅₀ greater than 500 mg bait/kg on both
intact and abraded skin

Acute Skin Irritation, rabbit: Erythema in one of 6 rabbits after
24 hours; essentially non-irritating

Primary Eye Irritation, rabbit: Slight corneal opacity in one of 6 rabbits
with unwashed eyes. Irrigation almost completely eliminates the
irritant response. Formulation classed as a mild irritant.

Handling Precautions: The dosage formulation requires no special precautions
in handling. The Liquid Concentrate Formulation has a dermal LD₅₀ of
1 ml/kg (or about 1000 mg/kg), so also is not exceedingly toxic by the
dermal route. However, persons engaged in the manufacturing operations
should not expose themselves excessively to the Liquid Concentrate
during the manufacturing process.

RECOMMENDATION: Toxicology Branch sees no reason why the EUP should not
be granted.

Roland A. Gessert

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